IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT INTERFERENCES

Moncada :

v. : Interference No. 100,116

Johnson, et al. :

To the Commissioner of Patents and Trademarks

Washington, D. C. 20231

DECLARATION UNDER MPEP 1105.02 IN SUPPORT OF JOHNSON MOTION TO DISSOLVE

ROY A. JOHNSON, being duly warned that willful false statements and the like are punishable by fine or imprisonment or both (18 USC 1001) and may jeopardize the validity of the Johnson, et al. application of the above-captioned interference or any patent issuing thereon, states and declares:

THAT all statements herein made of his own knowledge are true and that all statements herein made on information and belief are believed to be true;

THAT he received the Doctor of Philosophy degree in Organic Chemistry and Biochemistry from the University of Minnesota in 1965;

THAT since 1965 he has been employed by The Upjohn Company, Kalamazoo, Michigan, as a Research Scientist in the Experimental Chemistry Department;

THAT, during his employment with The Upjohn Company, he

has had extensive personal involvement in the prostaglandin research programs of The Upjohn Company and has undertaken the chemical synthesis and characterization of numerous prostaglandin-type compounds;

THAT since 1976 he has been involved in the research programs of The Upjohn Company relating to the discovery of prostacyclin;

THAT he is a co-inventor of the Johnson application in the above-captioned interference;

THAT he is a co-inventor of salts and derivatives of prostacyclin as is set forth in the count of the above-captioned interference;

THAT his invention of prostacyclin derivatives and analogs included the preparation by him or his co-workers on or about 7 July 1976 of prostacyclin methyl ester and the preparation by him or his co-workers on or about 2 August 1976 of prostacyclin sodium salt, in a free-flowing solid form

THAT these substances were prepared by him by wholly chemical means, independent of enzymatic or other biological processes from starting materials readily available to him;

THAT, in contrast to his invention of prostaglandin derivatives and analogs within the scope of the count, the invention of Moncada as described in United Kingdom Application Nos. 19384, 34151, 36547, filed respectively on

11 May, 17 August, and 3 September 1976, represents an essentially biological discovery of the microsomial conversion of prostaglandin endoperoxides to a residue designated as "PGX";

THAT this PGX product of the Moncada process is prepared, inter alia, by the incubation of certain microsomes in a tris buffer, followed by extraction in cold dry diethyl ether and concentration to a residue;

THAT one of ordinary skill in the art would anticipate that the extraction of prostaglandin-type substances from an aqueous solution into a dry diethyl ether solution would have resulted in the presence in the diethyl ether solution of preponderantly fatty free acids as opposed to the corresponding salts thereof;

THAT, as suggested by Moncada at page 5 of his Preliminary Statement, the extraction of some salts of fatty acids into diethyl ether theoretically could be possible when the diethyl ether solution is saturated with water;

THAT he can accept the statement by Moncada at page 5 of his Preliminary Statement to the effect that the PGX product of the Moncada process "would have consisted of prostacyclin and these [tris and sodium] salts" only with the following qualifications:

(a) the free acid form of any fatty acids present in the PGX product would probably have been present in great preponderance over the corresponding salt forms;

(b) to the extent that any metallic salts of such fatty acids would have been present in the PGX product, such as the sodium salt, likewise present in the PGX product would have been other fatty acid salts derived from metal ions ordinarily found in biological media, including potassium salts, calcium salts, magnesium salts, and numerous other salts;

(c) since diethyl ether extraction is a known and recognized means for extraction of fatty acids from aqueous media, all fatty acids present in the aqueous media are likely to have been extracted into the diethyl ether and to have been present in the residue obtained by Moncada as his PGX product;

(d) in all probability prostacyclin was obtained together with a mixture of other fatty acids in the PGX product of the Moncada process, since numerous fatty acids are present ordinarily in biological systems; and

(e) the PGX product of the Moncada process most probably contained prostacyclin and the novel biologically active principle of the PGX product was most probably preponderantly prostacyclin; but if one includes the possible presence of entities such as the tris and especially sodium salts, the PGX product must be considered to be a very complex mixture of substances;

THAT, given the extremely minute quantities of the PGX

product of the Moncada process which are biosynthetically produced, there were no means known to him then, nor are there means known to him now, by which chemically homogenous samples of prostacyclin or a salt thereof could be or can be isolated from the complex mixture of substances present in the PGX product of the Moncada process;

THAT, there has never been known to him, for example, the preparation of a chemically homogenous sample of a single fatty acid or a salt thereof from the PGX product of the Moncada process;

THAT, his reading of the aforementioned British applications and the Moncada Preliminary Statement in the above-captioned interference, including the exhibits thereto, make clear to him that, aside from the presence of a single active principal in the PGX product of the Moncada process, there was no contemporaneous appreciation by Moncada that this complex mixture of substances would have contained any appreciable or recognizable quantities of other novel pharmacological materials, most especially salt forms of fatty acids;

THAT he particularly notes the statement by Moncada on the 5th page of the Moncada Preliminary Statement which indicates with respect to the PGX product of the Moncada process that this product "would have consisted of prostacyclin and these salts" to be indicative of the fact

that within this complex mixture only the benefit of hindsight enabled Moncada to appreciate a complexity of the product;

THAT even the hypothesis that prostacyclin was the active principle of the PGX product of the Moncada process is not known by him to have been established prior to experiments undertaken by him in August of 1976 where he established the substantial chemical identity between a methyl ester prepared from the PGX product of the Moncada process and prostacyclin methyl ester prepared by him by means of a total chemical synthesis;

THAT, with respect to the complexity of the mixture of substances comprising the PGX product of the Moncada process, this complex mixture is characterized by the process of its manufacture, rather than by wholly chemical criteria, which stands in complete and total contrast to the invention by him and his co-workers which is fully and completely characterized by the chemical structure of substances prepared by purely chemical means;

THAT, based on his review of all the relevant facts, including a review of the Moncada file wrapper, Moncada Preliminary Statement and exhibits, his personal knowledge in dealing with Moncada and other personnel of the Wellcome Foundation, Ltd., he concludes that on and immediately prior to the filing of United States Serial No. 716,770 on

23 August 1976 that the following situation pertains:

(a) he and his co-workers had prepared and established striking biological activity for prostacyclin methyl ester and prostacyclin sodium salt;

(b) Moncada had established striking biological activity for the PGX product of the Moncada process;

(c) he and those working under his direction and control had established that a methyl ester of the PGX product of the Moncada process was chemically identical to prostacyclin methyl ester;

(d) Moncada had a clear appreciation of the existence of an active biological principal in the PGX product of the Moncada process, but did not recognize and did not appreciate the possibility that this PGX product would have included prostacyclin derivatives and analogs such as were invented by him and his co-workers and are within the scope of the count of the above-captioned interference;

(e) the PGX product of the Moncada process was not thought to have contained any appreciable amount and certainly did not contain any recognized amount of any derivative or analog of prostacyclin; and

(f) the PGX product of the Moncada process was generally accepted to consist of prostacyclin as its preponderant novel biologically active component;

THAT, therefore, in his opinion, the discovery of the PGX product of the Moncada process was a separate and independent scientific discovery from the invention by him and his co-workers of prostacyclin derivatives and analogs by chemical means;

THAT, in his opinion, the scientific connection between these discoveries was established only retrospectively, in that the identity of the PGX product of the Moncada process to the free acid form of prostacyclin was established only after the invention of him and his co-workers and the invention of Moncada had been completed;

THAT, the discovery of the PGX product of the Moncada process, including its relationship to prostacyclin, was a discovery of great and immediately recognized biological significance; and

THAT, likewise, he believes that the discovery by him and his co-workers of prostacyclin derivatives and analogs produced by chemical means was likewise an important and fundamental contribution to the prostaglandin field.

Roy A. Johnson

Roy A. Johnson

Date: June 12, 1979